

REMARKS

Claims 1, 3, 4 and 6-14 are pending in this application. In this Amendment, claim 5 has been canceled and claims 1 and 4 have been amended. Support for amended claims 1 and 4 is found in originally filed claims 5 and 4, respectively, for example. No new matter has been added by this Amendment.

I. Formal Matters

A. Objection under 35 U.S.C. §132 (new matter)

The Examiner objected to the Amendment filed July 28, 2003, under 35 U.S.C. §132 "because it introduces new matter into the disclosure" (Office Action, page 3). The Examiner stated that the phrase "a first molecule located on the solid support at a known position **within** the array" is not supported by the original disclosure. Applicants respectfully disagree with the Examiner's objection.

In response, without acquiescing in the propriety of the objection, but solely to expedite prosecution, Applicants have amended claim 1 such that the allegedly unsupported phrase is no longer found in the claim. Claim 1, as amended, requires that a first molecule is located on the solid support in a corner of the array.

In view of the amendment to claim 1, withdrawal of the objection is respectfully requested.

B. Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1 and 3-14 under 35 U.S.C. §112, first paragraph, for "failing to comply with the written description requirement" due to the allegedly unsupported phrase "a first molecule located on the solid support at a known position **within** the array" (Office Action, page 4). Applicants respectfully traverse the rejection.

In response, without acquiescing in the propriety of the objection, but solely to expedite prosecution, Applicants have amended claim 1 such that the allegedly unsupported

phrase is no longer found in the claim. Claim 1, as amended, requires that a first molecule is located on the solid support in a corner of the array.

In view of the amendment to claim 1, withdrawal of the rejection is respectfully requested.

C. Rejections under 35 U.S.C. §102(b)

1. The Examiner rejected claims 1, 4-10 and 14 under 35 U.S.C. §102(b) as being anticipated by Fiekowsky et al. (U.S. Patent No. 6,090,555) ("Fiekowsky"). Applicants respectfully traverse the rejection.

It is the Examiner's position that Fiekowsky discloses all of the claimed elements in the methods of claims 1, 4-10 and 14 (Office Action, pages 5-6).

In order for a reference to anticipate a claim, the reference must teach every element in the claim. Fiekowsky fails to anticipate every element of claims 1, 4, 6-10 and 14 for at least the reasons set forth below.

Regarding amended claim 1, upon which claims 4, 6-10 and 14 depend, the method claimed requires at least the following:

- 1) imaging an array of discrete reaction sites on the surface of a solid support;
- 2) aligning a first inspection window within a region of the solid support that includes a first molecule located in a corner of the array;
- 3) searching within the first inspection window to detect the first molecule;
- 4) detecting a signal from the first molecule;
- 5) using the first molecule as a reference point, aligning an individual inspection window in registration with each discrete reaction site; and
- 6) determining the amount of detectable signal in each inspection window, thereby detecting the presence of the molecules on the array.

Fiekowsky fails to disclose the above elements and instead describes a method of scanning images that requires a line-by-line scan to identify a reference pattern that is distinct from the array to be identified. Thus, when practicing the Fiekowsky method, one of ordinary skill in the art must use a reference pattern that is sufficiently separate from the array to obtain an analysis with a high degree of accuracy. If the reference pattern is part of the array, then false positive recognitions result. In contrast, Applicants' claimed method uses a reference point, i.e., first molecule, located in a corner of the array, i.e., the first molecule is part of the array.

Since Fiekowsky does not teach the use of a first molecule as part of the array and, more specifically, in a corner of the array, Fiekowsky does not teach each and every component of the claimed method, and thus does not anticipate claims 1, 4, 6-10 and 14.

In view of the arguments set forth above, Applicants respectfully request that the Examiner withdraw the rejection.

2. The Examiner rejected claims 1 and 4-10 under 35 U.S.C. §102(e) as being anticipated by Noblett (U.S. Patent No. 6,362,004) ("Noblett"). Applicants respectfully traverse the rejection.

It is the Examiner's position that Noblett discloses all of the claimed elements in the methods of claims 1 and 4-10 (Office Action, pages 6-7).

As noted above, in order for a reference to anticipate a claim, the reference must teach every element in the claim. Noblett fails to anticipate every element of the method of claims 1, 4 and 6-10 for at least the reasons set forth below.

Regarding amended claim 1, upon which claims 4 and 6-10 depend, the method claimed requires at least the following:

- 1) imaging an array of discrete reaction sites on the surface of a solid support;

- 2) aligning a first inspection window within a region of the solid support that includes a first molecule located in a corner of the array;
- 3) searching within the first inspection window to detect the first molecule;
- 4) detecting a signal from the first molecule;
- 5) using the first molecule as a reference point, aligning an individual inspection window in registration with each discrete reaction site; and
- 6) determining the amount of detectable signal in each inspection window, thereby detecting the presence of the molecules on the array.

Noblett fails to disclose the elements recited above and instead, describes a microarray analysis system that includes a fiducial mark for positioning and aligning a substrate. The fiducial mark, which reportedly improves the placement of the reaction sites on the microarray, is used to determine the relative coordinates of the reaction sites positioned on the microarray (col. 6, lines 29-63). Thus, the fiducial mark functions as a reference point.

Applicants note that the first molecule recited in claim 1 also functions as a reference point. However, Applicants' reference point is in a corner *of the array*, whereas Noblett's reference point is *not* in a corner of the microarray, but, as illustrated in Figures 2, 6 and 7, is placed at a separate and distinct location *away from* the microarray. Such a placement indicates that one of ordinary skill in the art practicing the Noblett method must have prior knowledge of the relative position between the fiducial mark, i.e., the reference point, and the other molecules of the microarray. The claimed method does not require such prior knowledge in view of the placement of the first molecule, i.e., reference point, in a corner of the array.

It is the Examiner's position that, although Noblett does not disclose the location of a fiducial mark "within the array," Noblett does disclose the location of a fiducial mark "on the array" (Office Action, page 8). The Examiner did not provide any support for this assertion

and Applicants have not located such support in the Noblett patent. The microarray in the Noblett patent is found *on* the substrate, which includes the glass microscope slide illustrated in Figure 2. Similarly, the fiducial marks are found *on* the substrate. However, the fiducial marks are *not* found on the microarray section of the substrate.

Since Noblett does not teach the location of a first molecule, i.e., reference point, as a part of the array and, more specifically, in a corner of the array, Noblett does not teach each and every component of the claimed method, and thus does not anticipate claims 1, 4 and 6-10.

In view of the arguments set forth above, Applicants respectfully request that the Examiner withdraw the rejection.

3. The Examiner rejected claims 1 and 3-11 under 35 U.S.C. §102(e) as being anticipated by Juncosa et al. (U.S. Patent No. 6,309,601) ("Juncosa"). Applicants respectfully traverse the rejection.

It is the Examiner's position that Juncosa discloses all of the claimed elements in the methods of claims 1 and 3-11 (Office Action, pages 8-9).

As noted above, in order for a reference to anticipate a claim, the reference must teach every element in the claim. Juncosa fails to anticipate every element of the method of claims 1, 3, 4 and 6-11 for at least the reasons set forth below.

Regarding amended claim 1, upon which claims 3, 4 and 6-11 depend, the method claimed requires at least the following:

- 1) imaging an array of discrete reaction sites on the surface of a solid support;
- 2) aligning a first inspection window within a region of the solid support that includes a first molecule located in a corner of the array;
- 3) searching within the first inspection window to detect the first molecule;
- 4) detecting a signal from the first molecule;

- 5) using the first molecule as a reference point, aligning an individual inspection window in registration with each discrete reaction site; and
- 6) determining the amount of detectable signal in each inspection window, thereby detecting the presence of the molecules on the array.

Juncosa does not teach the elements set forth above and instead teaches an optical detection system, which includes a confocal scanning system. The system disclosed by Juncosa does not detect a signal from a first molecule located on a solid support in a corner of an array, and does not use that first molecule to align an *individual* inspection window in registration with *each* discrete reaction site, as recited in claim 1. Juncosa discloses a system that uses *a single* inspection window, which covers the array of reaction sites.

It is the Examiner's position that Juncosa discloses "alignment in registration with each site" (Office Action, page 10). The Examiner referred to the Juncosa patent, column 10, lines 45-66, for support of such alignment. However, the passage relied upon by the Examiner refers to the positioning of a detector in proximity to an array and then scanning the array to detect radiation emission. The "alignment" recited in the passage does not refer to individual inspection windows and discrete reaction sites, but instead refers to the "object to be examined" (col. 10, lines 61-66). *See also* Juncosa, Figure 4, reference number 164. Disclosure of the required claim element of detecting a signal from a first molecule located on the solid support in a corner of the array and referencing that first molecule to align an *individual* inspection window in registration with *each* discrete reaction site is not found in Juncosa at column 10, lines 45-66, nor anywhere else in the patent.

Since Juncosa does not teach detecting a signal from a first molecule located on the solid support in a corner of the array *and* referencing that first molecule to align an *individual* inspection window in registration with *each* discrete reaction site, Juncosa does not teach

each and every component of the claimed method, and thus does not anticipate claims 1, 3, 4 and 6-11.

In view of the arguments set forth above, Applicants respectfully request that the Examiner withdraw the rejection.

D. Rejections under 35 U.S.C. §103(a)

1. The Examiner rejected claim 3 under 35 U.S.C. §103(a) as being unpatentable over Fiekowsky et al. (U.S. Patent No. 6,090,555) ("Fiekowsky") in view of Juncosa et al. (U.S. Patent No. 6,309,601) ("Juncosa"). Applicants respectfully traverse the rejection.

It is the Examiner's position that Fiekowsky discloses all of the claimed elements in the method of claim 1, but does not teach the claimed elements in the method of claim 3 (Office Action, pages 10-11). More specifically, the Examiner acknowledged that Fiekowsky does not teach searching carried out by scanning an array of pixels diagonally and determining their value as recited in claim 3. To remedy the defects of the primary reference, the Examiner cited Juncosa.

Juncosa is directed to an optical detection system, which includes a confocal scanning system. According to the Examiner, Juncosa teaches diagonal scanning at column 11, lines 18-20, and in Figure 6A. However, although Juncosa discloses scanning, there is no indication at column 11, lines 18-20, or in Figure 6A or anywhere else in the Juncosa patent, that the scanning can be diagonal scanning.

In addition to failing to teach or suggest diagonal scanning, Juncosa does not teach or suggest an imaging method that includes at least the following:

- 1) imaging an array of discrete reaction sites on the surface of a solid support;
- 2) aligning a first inspection window within a region of the solid support that includes a first molecule located in a corner of the array;
- 3) searching within the first inspection window to detect the first molecule;

- 4) detecting a signal from the first molecule;
- 5) using the first molecule as a reference point, aligning an individual inspection window in registration with each discrete reaction site; and
- 6) determining the amount of detectable signal in each inspection window, thereby detecting the presence of the molecules on the array.

Thus, regardless of the teachings of Juncosa, the combination of Fiekowsky and Juncosa would not have taught or suggested, and would not have rendered obvious, to one of ordinary skill in the art, the method of claim 1. Since claim 3 depends from claim 1, claim 3 also would not have been rendered obvious.

In order to render claims *prima facie* obvious, there must be, *inter alia*, a reasonable expectation of success of obtaining the claimed invention based on the recited combination of references. In this case, since neither reference teaches or even suggests the required elements of the method of claim 1, the likelihood of successfully obtaining the method of claims 1 and 3 by combining the references is extremely low. In the absence of a likelihood of success in obtaining the claimed invention, the applied art does not establish a *prima facie* basis for a rejection under 35 U.S.C. §103(a).

Since the references, alone or in combination, do not teach or suggest the particular method claimed, Applicants respectfully assert that no *prima facie* case of obviousness has been established, and withdrawal of the rejection is respectfully requested.

2. The Examiner rejected claims 11-13 under 35 U.S.C. §103(a) as being unpatentable over Fiekowsky et al. (U.S. Patent No. 6,090,555) ("Fiekowsky") in view of Pirrung et al. (U.S. Patent No. 5,143,854) ("Pirrung"). Applicants respectfully traverse the rejection.

It is the Examiner's position that Fiekowsky discloses all of the claimed elements in the method of claim 1, but does not teach the claimed elements in the methods of claims 11-

13 (Office Action, pages 11-12). More specifically, the Examiner acknowledged that Fiekowsky does not teach that the solid support is less than 1 cm^2 , that the solid support is a ceramic, silicon or glass material or that the molecules of the array are covalently attached to the surface of the solid support. To remedy the defects of the primary reference, the Examiner cited Pirrung.

Pirrung is directed to photolithographic solid phase synthesis of polypeptides and to receptor binding screening thereof. According to the Examiner, Pirrung teaches using VLSIPS™ technology with a substrate made of silicon or glass of less than 1 cm^2 , wherein molecules are covalently attached to the substrate.

Pirrung does not teach or suggest an imaging method that includes at least the following:

- 1) imaging an array of discrete reaction sites on the surface of a solid support;
- 2) aligning a first inspection window within a region of the solid support that includes a first molecule located in a corner of the array;
- 3) searching within the first inspection window to detect the first molecule;
- 4) detecting a signal from the first molecule;
- 5) using the first molecule as a reference point, aligning an individual inspection window in registration with each discrete reaction site; and
- 6) determining the amount of detectable signal in each inspection window, thereby detecting the presence of the molecules on the array.

Thus, regardless of the teachings of Pirrung, the combination of Fiekowsky and Pirrung would not have taught or suggested, and would not have rendered obvious, to one of ordinary skill in the art, the method of claim 1. Since claims 11-13 depend from claim 1, claims 11-13 also would not have been rendered obvious.

In order to render claims *prima facie* obvious, there must be, *inter alia*, a reasonable expectation of success of obtaining the claimed invention based on the recited combination of references. In this case, since neither reference teaches or even suggests the required elements of the method of claim 1, the likelihood of successfully obtaining the method of claims 1 and 11-13 by combining the references is extremely low. In the absence of a likelihood of success in obtaining the claimed invention, the applied art does not establish a *prima facie* basis for a rejection under 35 U.S.C. §103(a).

Since the references, alone or in combination, do not teach or suggest the particular method claimed, Applicants respectfully assert that no *prima facie* case of obviousness has been established, and withdrawal of the rejection is respectfully requested.

3. The Examiner rejected claims 12-14 under 35 U.S.C. §103(a) as being unpatentable over Juncosa et al. (U.S. Patent No. 6,309,601) ("Juncosa") in view of Trulson et al. (U.S. Patent No. 5,578,832) ("Trulson"). Applicants respectfully traverse the rejection.

It is the Examiner's position that Juncosa discloses all of the claimed elements in the method of claim 1, but does not teach the claimed elements in the methods of claims 12-14 (Office Action, pages 12-14). More specifically, the Examiner acknowledged that Juncosa does not teach that the solid support is a ceramic, silicone or glass material, that the molecules of the array are covalently attached to the surface of the solid support, or that the signal detected in step (i) must be above a pre-defined value. To remedy the defects of the primary reference, the Examiner cited Trulson.

Trulson is directed to a method of imaging molecules. However, Trulson does not teach or suggest an imaging method that includes at least the following:

- 1) imaging an array of discrete reaction sites on the surface of a solid support;
- 2) aligning a first inspection window within a region of the solid support that includes a first molecule located in a corner of the array;

- 3) searching within the first inspection window to detect the first molecule;
- 4) detecting a signal from the first molecule;
- 5) using the first molecule as a reference point, aligning an individual inspection window in registration with each discrete reaction site; and
- 6) determining the amount of detectable signal in each inspection window, thereby detecting the presence of the molecules on the array.

Thus, regardless of the teachings of Trulson, the combination of Juncosa and Trulson would not have taught or suggested, and would not have rendered obvious, to one of ordinary skill in the art, the method of claim 1. Since claims 12-14 depend from claim 1, claims 12-14 also would not have been rendered obvious.

In order to render claims *prima facie* obvious, there must be, *inter alia*, a reasonable expectation of success of obtaining the claimed invention based on the recited combination of references. In this case, since neither reference teaches or even suggests the required elements of the method of claim 1, the likelihood of successfully obtaining the method of claims 1 and 12-14 by combining the references is extremely low. In the absence of a likelihood of success in obtaining the claimed invention, the applied art does not establish a *prima facie* basis for a rejection under 35 U.S.C. §103(a).

The Examiner's position regarding the alleged disclosure in Juncosa of "alignment in registration with each site" (Office Action, pages 10 and 14) is addressed above.

Since the references, alone or in combination, do not teach or suggest the particular method claimed, Applicants respectfully assert that no *prima facie* case of obviousness has been established, and withdrawal of the rejection is respectfully requested.

II. Miscellaneous

An Information Disclosure Statement with Form PTO-1449 was filed in the above-captioned patent application on October 27, 2003. Applicants have not yet received from the

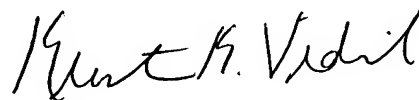
Examiner a copy of the Form PTO-1449 initialed to acknowledge the fact that the Examiner has considered the disclosed information. The Examiner is requested to initial and return to the undersigned a copy of the Form PTO-1449. For the convenience of the Examiner, a copy of that form is attached.

III. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1, 3, 4 and 6-14 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



James A. Oliff
Registration No. 27,075

Kristin K. Vidovich
Registration No. 41,448

JAO/KKV:amw

Attachment:
Form PTO-1449

Date: April 14, 2004

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

<p>DEPOSIT ACCOUNT USE AUTHORIZATION Please grant any extension necessary for entry; Charge any fee due to our Deposit Account No. 15-0461</p>
--